

BRILLIANT GREEN

A CLINICAL STUDY OF ITS VALUE AS A LOCAL ANTISEPTIC

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AN IDEAL local antiseptic must meet several requirements and possess the following properties:

1. Great inhibitory power toward pathogenic microorganisms, at least those which are most important and most frequently encountered in common surgical diseases; this antiseptic property must be exhibited not only *in vitro* but also *in vivo*, *i.e.*, in the presence of serum.
2. Rapidity of action, in order to prevent spreading of infection.
3. Sufficient penetrating power.
4. No deleterious effects on phagocytosis, products of glandular secretion, hormones and other defensive processes of the organism.
5. Absence of irritating effects, even after repeated applications upon the tissues of the host, including delicate and sensitive structures such as mucous membranes.
6. No interference with or a stimulating effect upon reparation processes of the organism, particularly formation of granulation tissue.
7. Low toxicity in case of absorption.

Generally speaking the local antiseptics can be divided into two groups: (1) Those which are not irritating and injurious to the tissues but have an extremely low germicidal action. (2) Those which are powerful disinfectants but at the same time damage the tissues. Their action as irritants arises from the same qualities as their bactericidal or bacteriostatic power, namely from general toxicity to the living matter.

Certain objectionable characteristics confine the justifiable application of most of the popular antiseptics to within narrow limits. For instance, acriflavin has won favor because of its penetrating action and the length of its activity, but it is not a particularly rapidly acting antiseptic. This fact lessens its value for prophylactic treatment of potentially infected wounds. Hexylresorcinol gave growth of bacteria in all tests carried out by Raisiss and Severac.¹ Tincture of iodine has the disadvantage of causing irritation of the skin in many patients, particularly if wet compresses have to be applied after painting with iodine. Tinker and Sutton² found that iodine, trinitrophenol, Harrington's mercuric chloride solution, mercurochrome—220 soluble—and potassium mercuric iodide will not kill most of the resistant bacteria and some of the less resistant pathogenic bacteria under conditions of perfect contact.

It is exceedingly difficult to estimate the value of an antiseptic in the

prevention or treatment of septic processes because the innumerable bacteriological tests at our disposal are all subject to criticism; hence the reports are confusing and contradicting. Practically speaking, the only method to judge an antiseptic, after its bactericidal action has been ascertained in preliminary antiseptic and toxicity tests, is to evaluate the clinical results obtained and to compare them with results observed after use of other known disinfectants.

The fact that new antiseptics and germicidals make their appearance in the literature and on the market serves as best proof that most of the substances in general use fall short of the ideal in their therapeutic action. The popularity of some of the newer antiseptics is not based entirely upon their merits but is due partially to the wide publicity and undiscerning enthusiastic reports.

On the other hand, some valuable old antiseptics have been overlooked or fallen into misuse either because they have not been made the subject of extensive clinical studies or because they did not represent products of high commercial value. One of the most powerful among such antiseptics is brilliant green. The bacteriostatic action of certain dyes on bacteria was observed as early as 1887. Browning, *et al.*³ recommended the use of brilliant green in 1917; they found that the substance is particularly destructive to the cocci group but toward bacterium coli its bactericidal value is considerably lower. Krumwiede and Pratt⁴ found that the inhibition of growth by brilliant green has been most evident among the Gram-positive bacteria; the paratyphoid enteritidis types are more resistant. Ligat⁵ reported very satisfactory results with brilliant green. Peterson⁶ studied the comparative merits of various antiseptics by recording their inhibiting effect upon the yeast-sugar mixture. The method consists in determining the smallest quantity of drug that will prevent the formation of gas in a yeast-sugar mixture of definite strength during a period of one hour. Whereas the inhibitory amount of metaphen in grams was 0.0017 and that of mercurochrome 0.065, the amount of gentian violet was only 0.0039, crystal violet 0.0024 and methyl violet 0.0051. These figures show that the above-mentioned aniline dyes possess a much stronger inhibitory power than mercurochrome and compare very favorably with metaphen. Another dye, however, is still superior to these aniline dyes as far as bactericidal action is concerned and this is brilliant green as shown by the experiments carried out by Norton and Davis⁷ who determined the bacteriostatic action of dyes on streptococcus viridans and pneumococci. They state that brilliant green is the most active dye they found, as evidenced from the following part of their protocol:

Dye	Slightest dilution giving complete inhibition
Brilliant green	200,000
Gentian violet	40,000
Methylene blue	25,000
Methyl violet	10,000

According to their statement to have a marked bacteriostatic action, a dye must contain three benzol rings and two or more amino-groups in which the

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hydrogen atoms have been substituted by alkyl radicals. In most instances this alkyl radical is the methyl group but in brilliant green ethyl groups are present.

Disregarding the excellent qualifications, brilliant green has fallen into oblivion and the interest in it was revived by Doctor Baccal,^{8, 9} the scientific collaborator of the surgical clinic of the State Institute of Odessa. He limited his report to general statements as to the great value of brilliant green in minor surgery, pre-operative preparation of the skin, sterilization of hands, catgut and surgical instruments and treatment of burns and certain external eye diseases, such as blepharitis.

In view of the above-mentioned laboratory experiments and favorable clinical reports by Browning, Ligat, Baccal and others, a further investigation of the qualities of brilliant green seemed to be justified. The present study was limited to evaluation of brilliant green as a local antiseptic.

Brilliant green chemically is a diamino-triphenylmethane compound. The product is a green powder, soluble in water and alcohol; the aqueous solution is not stable and should be freshly prepared; it has been used by me only for warm baths and compresses. Otherwise a 1 per cent. solution in 60 per cent. alcohol was used in all the cases except mucous membranes where 0.5 per cent. solution seemed to be more advisable. The stains on hands can be removed by vigorous rubbing with alcohol or hydrogen peroxide; the latter can be used to remove stains from soiled linen, but usually the ordinary washing processes are sufficient.

As space prevents a detailed report of all cases treated, a brief résumé shall be made of the clinical results obtained. The treatment was either prophylactic or therapeutic.

A. Prophylactic Treatment with Brilliant Green.—1. Pre-operative Preparation of the Skin: a. Minor surgery.—Unless exceptionally dirty when a preliminary washing with soap and water was necessary, no preparation of the skin except painting with 1 per cent. brilliant green solution was made in order to form a better judgment as to the antiseptic power of the product. Operations were performed for such conditions as subcutaneous lipomas, fibromas, cystomas of the tendon sheaths, sebaceous cysts, phimosis, etc. In infants 0.5 solution was used instead of 1 per cent. solution. The results obtained in this group were very satisfactory. In the whole series of ninety-three cases there was not a single occurrence of infection. The great susceptibility of the tendon sheaths to infection is well known; nevertheless in seven cases of ganglion of the tendons no infection occurred. An irritation of the skin could not be observed in any of the above-mentioned cases.

b. Major Surgery.—After the favorable results obtained in the pre-operative treatment of minor cases, the use of brilliant green in major surgery seemed to be justified. After the routine preparation, consisting of washing with soap and water, followed by alcohol, a 1 per cent. alcoholic solution of brilliant green was used for the pre-operative preparation of the skin in laparotomies for various conditions. The results were highly satisfactory.

No infections were observed which could be ascribed to the use of brilliant green. In one case a stitch abscess occurred which could be traced to contaminated catgut. Not in a single case in the series of III were there any indications of irritation of the skin, even when wet compresses had to be applied afterward. The use of brilliant green should be of special value in the pre-operative preparation of the skin for thyroidectomies where absorption of the tincture of iodine is feared. A 0.5 per cent. solution was used on mucous membranes for hemorrhoidectomies, vaginal repairs, suturing of lacerated lips and similar conditions.

2. *Prophylactic Treatment* of potentially infected wounds and abrasions including minor injuries as well as extensive lacerations which came under treatment a very short time after injury and where no clinical signs of infection were yet present. There is no positive criterion to judge the efficiency of an antiseptic in such conditions and in forming an opinion one is guided by impressions rather than by definite figures. An opportunity presented itself, however, in a case of laceration of several fingers to investigate the comparative value of metaphen, mercurochrome and brilliant green. All seven injured fingers presented approximately the same degree of injury of soft parts and were equally contaminated with dirt and machine oil. The two wounds treated with metaphen showed no signs of infection and produced granulations of a pale pink color; the healing process was fairly rapid; three fingers treated with mercurochrome produced pus and showed brownish granulations of moderate size with very slow healing tendencies; in two fingers treated with brilliant green a rapid formation of exuberant, bright-red granulations could be observed which led to a scar formation more quickly than in the other fingers. Of course, such an experiment is not conclusive as to the relative value of various antiseptics as it may be argued that the degree of infection of each injured finger could not be exactly determined; nevertheless the striking results are in line with experiments of Browning, *et al.*,³ who also observed in a large number of cases that brilliant green stimulates the formation of richly vascularized red granulations while with flavine the granulations were not so bulky and of pale color. No indications of tissue damage or irritation could be observed.

B. *Therapeutic Treatment*.—This category comprises 123 cases which already exhibited manifest infection when they presented themselves for treatment. This group comprises such spastic conditions as abscesses located in various parts of the body, including Bartholini's abscesses and post-operative stitch abscesses; acute suppurative bursitis; acute suppurative lymphadenitis; boils; carbuncles; phlegmons, cellulitis; fistulæ resulting from osteomyelitis. In addition to the painting of the skin with brilliant green solution before the incision was made, the solution was also instilled into the wounds at each dressing. In a number of cases this treatment was supplemented by bathing the infected part in a warm aqueous solution of brilliant green 1:2000 and compresses of an aqueous solution 1:1000. In ischio-rectal and perianal abscesses the results appeared to be superior to mercuro-

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chrome but to an impartial eye they were not better than those obtained with acriflavine and especially with metaphen; the same observation was made in abscesses after appendectomies and in cold abscesses. This fact is probably due to the above-mentioned limitations of the bactericidal properties of brilliant green. As stated, this chemical is very efficient in all cocci infections but its antiseptic power is much smaller toward bacterium coli and tubercle bacilli. In the rest of the cases the results ranged from very satisfactory to excellent.

Discussion.—The clinical results with brilliant green solution as local antiseptic showed that the product was efficient as a prophylactic measure against infection in the pre-operative preparation of the skin. In the treatment of infected wounds and various septic processes the impression was gained that the infection was more quickly brought under control, the granulations were more abundant and healthier and the healing process was more rapid than has been the author's experience with other antiseptics in general use. As to the toxicity, no ill effects following the use of this substance over prolonged periods of time could be observed. It is left to the genito-urinary specialists to decide whether a clinical trial with brilliant green in the treatment of gonorrhoea is desired. As to the intravenous injections, extensive laboratory experiments will be necessary. The use of brilliant green for sterilization of the hands of the surgeon as advocated by Baccal will hardly become popular in view of the staining properties of the substance. The attempt to use it in preparation of catgut may be justified although several manufacturers asserted to the author that there is no need for introduction of a new antiseptic in preparation of catgut as the present methods are satisfactory. A recent report by Meleney and Chatfield¹⁰ shows that in a study of 174 specimens of catgut submitted by twelve surgical clinics, twenty-two or 12½ per cent. were found to yield spore-forming bacteria including the common gas gangrene organisms. In this connection it may be interesting to note that according to Churchman¹¹ who studied the bacteriostatic action of gentian violet upon bacterium anthracis, the spores are at least gravely affected by treatment with the dye and that in presence of it they can not develop. As brilliant green has a higher bacteriostatic action than gentian violet, the use of it may be of value in preparation of catgut. A ¼ per cent. ointment prepared by dissolving brilliant green in water and mixing it with petrolatum has been recommended by Baccal for treatment of burns.

SUMMARY

A survey of the clinical results after the use of brilliant green as local antiseptic in prophylaxis as well as treatment of various surgical conditions shows that the substance possesses a high antiseptic value toward the most frequent pathogenic microorganisms encountered in surgical diseases; it has an excellent power of penetration; it is non-irritant and non-toxic; it stimulates the formation of healthy granulation tissues and, last but not least, it is

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very cheap. The impression was gained that in many instances the substance was superior to other antiseptics in common use. These findings justify further clinical investigations as to the value of brilliant green and suggest the desirability of laboratory experiments in order to evaluate it as a general antiseptic.

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